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# Randomized Trial of 2 Self-Titrated Oral Appliances for Airway Management

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**Abstract**

The effectiveness and predictability of 2 different oral appliance (OA) designs to reduce the respiratory event index (REI) in moderate and severe obstructive sleep apnea (OSA) patients requires elucidation. The primary aim of the trial was to determine if 2 widely used midline-traction and bilateral-thrust OA designs differ in effectiveness to reduce the REI within a single test population categorized by OSA severity. Moderate and severe adult OSA patients, who were previously prescribed continuous positive airway pressure therapy (CPAP) but were dissatisfied with it ($n = 56$), were studied by home-polygraphy in a randomized crossover trial using either midline-traction with restricted mouth opening (MR) or bilateral thrust with opening permitted (BP) design OAs. OAs were used nightly for 4 wk (T2) followed by a 1-wk washout period, then 4 wk (T4) using the alternate OA. REI and oxygen saturation ($SaO_2$) were primary outcomes, while predictability and efficacy comparison of the 2 OAs were secondary outcomes. Thirty-six participants had used MR and BP OAs during both 4-wk study legs. Twenty (55.6%) MR OA-using participants, 25 (69.4%) BP OA-using participants, and 16 (44.4%) participants using both OAs had significant REI reductions. Overall baseline (T0) median REI (interquartile range) of 33.7 (20.7–54.9) was reduced to 18.0 (8.5–19.4) at T2 and to 12.5 (8.2–15.9) at T4 ($P < 0.001$). Comparison of the 2 sequence groups' (MR-BP and BP-MR) REI showed the median differences between T0 and T2 and T4 were highly significant ($P < 0.001$). Regression analysis predicted about half of all users will have REIs between 8 and 16 after 2 mo. Baseline overjet measures >2.9 mm predicted greater OA advancement at T4. Mean and minimum $SaO_2$ did not change significantly from T0 to T2 or T4. MR and BP OA designs similarly attenuated REI in moderate and severe OSA individuals who completed the 8-wk study protocol with greater REI reduction in those with severe OSA (ClinicalTrials.gov NCT03219034).

**Keywords:** obstructive sleep apnea, respiratory tract, occlusal splints, comparative effectiveness research, crossover studies, polysomnography

## Introduction

Obstructive sleep apnea (OSA) has an estimated prevalence of 5% to 38% in the general adult population (Punjabi 2008; Senaratna et al. 2017; Appleton et al. 2018). Continuous positive airway pressure (CPAP) is the American Academy of Sleep Medicine (AASM) option for this prevalent disorder (Berry et al. 2012). However, approximately 15% to 60% of patients with OSA do not adhere to CPAP therapy (Hoekema, Stegenga, et al. 2007). An alternative treatment option for OSA is oral appliance therapy (OAT), which functions to open the airway by bringing the mandible and tongue forward, but its effectiveness in moderate and severe OSA has been debatable.

Oral appliances (OAs) that advance the mandible but permit mouth opening may be less effective in attenuating OSA (Ghazal et al. 2009; Zhou and Liu 2012; Marklund 2017). Such reductions in efficacy may be related to more posterior tongue movement and greater soft tissue collapse during sleep, decreasing the oropharyngeal space (Hu 2018). Contrastingly, several randomized clinical trials (RCTs; Rose et al. 2002; Lawton et al. 2005; Bishop et al. 2014; Norrhem and Marklund 2016) do not support this and thus need further testing.

OAT efficacy in OSA of different severities is also controversial. Of 14 RCTs comparing OA designs in a systematic review (Ahrens et al. 2011), only 2 (Gotsopoulos et al. 2002; Walker-Engström et al. 2003) included adequate samples of severe OSA patients to draw conclusions; success rates in these studies were sufficiently high to warrant further comparison of apnea-hypopnea index (AHI) attenuation in moderate versus severe OSA.

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A supplemental appendix to this article is available online.

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Previous reports using a custom-fitted, dentist-titrated midline-traction OA found large improvements in Epworth Sleepiness Scale (ESS) and Short Form–36 Health Survey (SF-36) scores, oxygen saturation ($SaO_2$) levels, and the AHI in patients with severe OSA after 12 wk of use (Hoekema, Stel, et al. 2007). Three RCTs and 2 other reports also used the same midline-traction device in patients with moderate and severe OSA (Hoekema, Stegenga, et al. 2008; Hoekema, Voors, et al. 2008; Deane et al. 2009; Ghazal et al. 2009; Holley et al. 2011). AHI improvements ranged from 80% to 90%. In contrast, several studies in patients with moderate and severe OSA using a bilateral-thrust design OA failed to demonstrate an AHI reduction to <10 events/h; they did, however, show >50% AHI reductions (mean, 55.4%; range, 53%–57%) from baseline conditions (Mehta et al. 2001; Gotsopoulos et al. 2002, 2004; Naismith et al. 2005).

We compared 2 widely used designs that differ in mouth-opening range and have been studied extensively but not in a single population. The primary aim was to test whether these OA designs differed in reducing the respiratory event index (REI) based on different criteria and $SaO_2$ stabilization. Secondary outcomes included efficacy comparison in patients with moderate versus severe OSA over a 9-wk test period, predictability of OA efficacy, self-reported responses to OAT effect on daytime sleepiness, and quality-of-life scores. Further information on the background to this study is presented in the Appendix.

## Methods

This RCT used a crossover design, was approved by the Institutional Review Board at Texas A&M University College of Dentistry (IRB#2017-0390-CD-FB), and was performed at this clinical facility. All adult (≥18 y old) participants were previously diagnosed by polysomnography (PSG) with moderate or severe OSA, expressed dissatisfaction with their prescribed CPAP therapy, and were amenable to trying OAT. Pre-enrollment PSG AHI values ≥15 and ≤30 and >30 events/h were used to categorize participants as having moderate or severe OSA, respectively. All inclusion/exclusion criteria and details regarding the protocol, primary variables, and secondary variables are presented in the Appendix. All subjects provided written informed consent.

The dentists on the team performed the oral examination, recorded key dental parameters, and obtained polyvinyl siloxane impressions (Defend Super Hydrophilic Impression Material), which were sent to the manufacturers' laboratories for custom fabrication using an occlusal record that was obtained at 60% of the patient's maximum protrusion. Fabrication was done prior to the participant's second appointment (T1) to ensure that problems with fit could be addressed prior to delivery. At T1, each subject was assigned to start with 1 of the 2 OAs. The randomization sequence was generated using Online Research Randomizer software, V4 (Urbaniak and Plous 2013). Dentists received the OAs in concealed envelopes with participants' coded identity numbers prior to fitting. The data analyst and somnologist were blinded to OA sequence. Masking the identities of the OAs from the participants was not possible due to obvious differences in design and color.

The TAP1 (AMI) and SomnoDent Flex (SomnoMed) were chosen as exemplars of midline-traction, restricts-opening (MR) and bilateral-thrust, permits-opening (BP) designs, respectively. Anteriorly, the MR has a midline hook that engages the upper with the lower tray and an adjustable screw; this anterior hinge-like mechanism restricts mouth opening. The BP uses side fins as anchors to move the lower tray forward with left- and right-side adjustable screws; these fins can be disengaged during use, allowing complete mouth opening.

One OA was used nightly for 4 wk followed by a 1-wk washout period, then 4 wk using the alternate OA. During the washout period, the participants were instructed to use their CPAP machines nightly. Participants were instructed to advance their mandibles based on each manufacturer's guidelines as follows: for the MR, 1 turn (0.3 mm each) per night and for the BP, 2 to 3 (0.1 mm each) turns bilaterally per night during the test period if snoring, observed OSA events, or daytime sleepiness persisted and if they did not experience discomfort. Subjects were invited to attend the clinic to have a team dentist assist in this titration process.

Home sleep recordings were collected using the NOX T3 recorder (NOX Medical). $SaO_2$ was measured with a finger probe pulse oximeter (Nonin Medical). All sleep recordings were collected in the subject's home sleep environment, and each subject received instructions on how to self-apply sensors. A minimum of 5 recorded hours without artifact was considered acceptable. All apnea and hypopnea events were visually scored using AASM 2007 scoring criteria (Berry et al. 2012). The Epworth Sleepiness Scale (ESS) and the Short-Form 36 (SF-36) were used to assess daytime sleepiness and health-related quality of life, respectively. Questionnaires were self-administered.

### *Statistical Analysis*

SPSS v25 software (SPSS, Inc.) was used for data analysis. Most of the sleep studies and survey variables were nonnormally distributed, so that frequencies, medians, and interquartile ranges (IQRs) were used for description. Normally distributed variables were summarized with means and standard deviations. Differences in frequencies were analyzed using chi-square and McNemar tests. The nonparametric Friedman 2-way analysis of variance (ANOVA) followed by Bonferroni-corrected Wilcoxon signed rank tests were used for testing differences among and between time points, respectively; Mann-Whitney tests were used for evaluating differences in between-group continuous variables; Spearman correlations were used to evaluate the relationship between certain dental and sleep measures. Linear and robust regression (Hayes and Cai 2007) was used to evaluate REI and related variables as a function of treatment time, as well as predictability of response to OAT. An $\alpha$ error level <0.05 was used throughout.

Power analysis determined that 38 participants were needed to yield a power of 0.90 with $\alpha = 0.05$ and an expected effect size of at least a 10-point difference in the end-of-treatment

**Table 1.** Baseline Characteristics of Participants by Oral Appliance Sequence Group ($n = 56$).

| | All | | MT-BT | | BT-MT | | |
|---|---|---|---|---|---|---|---|
| Characteristic | Median | IQR | Median | IQR | Median | IQR | *P* Value |
| Age, y | 61 | 51.0–68.0 | 64.5 | 46.3–69.0 | 61.0 | 52.0–66.0 | 0.523 |
| Sex, % male | 71.4 | | 56.0 | | 83.9 | | 0.016 |
| Ancestry, % European | 76.8 | | 79.2 | | 77.4 | | 0.491 |
| BMI, kg/m$^2$ | 31.0 | 27.9–33.8 | 30.3 | 27.4–34.0 | 31.0 | 28.0–33.6 | 0.519 |
| REI, no/h | 33.7 | 20.7–54.9 | 32.6 | 17.9–41.8 | 36.1 | 22.3–57.9 | 0.284 |
| Mean $SaO_2$ | 93.0 | 91.0–95.0 | 93.0 | 92.0–94.6 | 93.1 | 91.0–95.4 | 0.441 |
| Minimum $SaO_2$ | 80.0 | 77.0–85.0 | 80.0 | 76.0–85.0 | 82.0 | 77.0–87.0 | 0.554 |

Between-groups differences in sex and ethnic distribution were tested with chi-square. All others variables were analyzed with Mann-Whitney test. Ancestries of the non-European subjects were 12.5% Hispanic, 7.1% African and 3.6% Asian.
BMI, body mass index; BP, bilateral-thrust, permits-opening device; IQR, interquartile range (25%–75%); MR, midline-traction, restricts-opening device; REI, respiratory event index; $SaO_2$, oxygen saturation.

mean REI scores based on previous work (Lawton et al. 2005; Pogach et al. 2012; see Appendix).

## Results

### *Subjects*

From the screened cohort of 152 adults, 62 (41%) received an interview, of whom 56 (90.3%) were enrolled (Fig. 1). The distribution of baseline characteristics by group assignment, MR-BP versus BP-MR sequences, is shown in Table 1. There were no significant group differences with regard to age, ancestry, body mass index (BMI), REI, and mean or minimum $SaO_2$ ($P > 0.41$). Group BP-MR had a greater proportion of male participants (83.9% vs. 71.4%, $P = 0.016$). Self-reported ancestries were as follows: 43 European/White (76.8%), 4 Hispanic (12.5%), 7 African (7.1%), and 2 Asian (3.6%).

There were no significant baseline-differences between moderate ($n = 25$; 44.6%) and severe OSA ($n = 31$; 55.4%) subjects with regard to age, BMI, or mean $SaO_2$ ($P > 0.45$). Forty-two (75%) participants completed the first leg of the study. An additional 6 participants (10.7%) were lost during the washout phase due to lack of communication with the study coordinator. Thirty-six participants (64.3%) completed the second leg of the study, consisting of 24 males (BMI: $29.6 \pm 3.16$) and 12 females (BMI: $29.7 \pm 3.89$). Those who completed did not differ significantly from dropouts in baseline median REI (32.6 [18.8–48.5] vs. 36.0 [21.7–56.3]; $P = 0.724$) and mean or minimum $SaO_2$ ($P \geq 0.085$). No major adverse events related to the use and titration of OAs were reported. See Appendix for the dentofacial assessment of the subjects at baseline and OA titration details. None of these variables significantly predicted primary or secondary outcome variables.

### *Response to OA Treatment*

*REI.* Within each OA sequence, the Friedman ANOVA omnibus test found significant differences among the time points in REI ($P < 0.001$; Fig. 2). Follow-up post hoc Wilcoxon tests showed REI reduced significantly from T0 to T2 and from T0 to T4 ($P < 0.001$). Other between- and within-group differences in REI and $SaO_2$ were not significant (Table 2).

The combined study group's REI variability reduced progressively over the 9 wk from a baseline IQR of 34.2 (T0) to 20.9 (T2) to a low of 7.7 events/h (T4). Friedman ANOVA demonstrated that these distributions differed significantly ($P < 0.001$) for the combined and separate groups. Absolute ranges similarly reduced at T4, excluding the 3 outliers.

"Responders" to a given OA had baseline REI reduced by ≥50% or REI <10 events/h at 4 wk. Thirty-six subjects used either MR or BP OAs during both 4-wk legs of the study. Twenty (55.6%) participants responded positively to the MR, 25 (69.4%) responded to the BP OAT, and 16 (44.4%) responded to both OATs. McNemar's test showed no significant differences between the 2 OATs in reducing REI over 4 wk ($P = 0.211$).

*Regression Analysis of REI as a Function of OA Treatment Over time.* Separate linear regressions were performed for the 2 OA sequence groups, as well as for the 2 OSA severity groups. There were no significant differences between the OA groups with regard to REI regression coefficients during either leg of the study ($P > 0.05$). The 2 OA groups were then combined to test the effects of severity. The decline in slopes of the regressions for the severe group was significantly steeper versus the moderate group ($P < 0.05$) during each leg of the study. $R^2$ values during leg 1 were 0.047 and 0.456 for moderate and severe OSA groups, respectively (Appendix Fig. 1), and $R^2$ values for leg 2 were 0.236 and 0.566 for these 2 groups, respectively (Fig. 3). All of these regressions except for the moderate OSA group during leg 1 were highly significant ($P < 0.001$). Robust regression was also performed due to heteroscedasticity. Adjusted standard errors yielded by this procedure did not alter interpretation.

*Overjet and Mandibular Advancement.* Baseline overjet was highly correlated with median amount of total mandibular advancement (TMA) at T2 and T4 ($\rho = 0.640$, $P < 0.001$; $\rho = 0.448$, $P = 0.009$). Overjet was significantly correlated with snore count at T4 ($\rho = -.593$, $P = 0.007$), but neither OJ nor

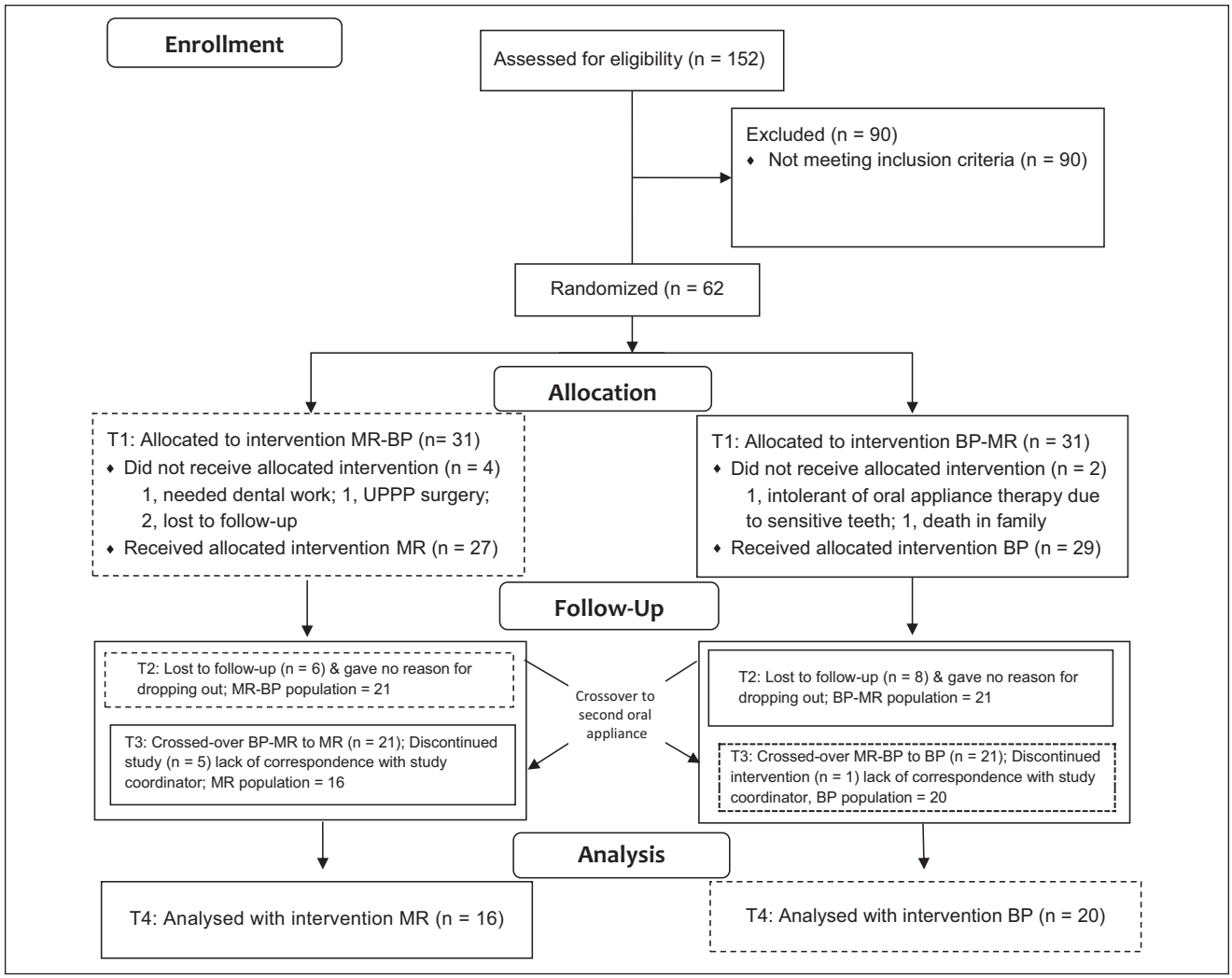


**Figure 1.** Study flow diagram with attrition.

**Table 2.** Sleep Test Results by Oral Appliance Sequence Group.

| | | | | | | | *P* Value | | |
|---|---|---|---|---|---|---|---|---|---|
| | All | | MR-BP | | BP-MR | | Between Groups | Within Groups from T2 to T4 | |
| Characteristic | Median | IQR | Median | IQR | Median | IQR | | MR-BP | BP-MR |
| REI at T0 | 35.3 | 20.5–50.6 | 29.8 | 18.0–39.3 | 38.7 | 21.3–57.6 | 0.170 | | |
| REI at T2 | 18.0 | 8.5–29.4 | 12.8 | 7.5–26.7 | 21.1 | 9.8–31.2 | 0.152 | 0.401 | 0.691 |
| REI at T4 | 12.5 | 8.2–15.9 | 9.3 | 7.7–15.5 | 13.1 | 10.4–16.6 | 0.232 | | |
| REI Δ T0 to T2 | 17.3 | ±22.8 | 17.0 | ±25.0 | 17.6 | ±20.8 | 0.929 | 0.152 | 0.883 |
| REI Δ T0 to T4 | 22.6 | ±23.0 | 25.3 | ±25.1 | 19.4 | ±20.6 | 0.853 | | |
| Mean $SaO_2$ at T0 | 93.2 | 92.0–95.0 | 92.0 | 92.0–94.8 | 94.0 | 91.1–96.0 | 0.338 | | |
| Mean $SaO_2$ at T2 | 93.0 | 91.6–93.8 | 92.3 | 91.5–93.7 | 93.1 | 91.6–93.9 | 0.505 | 0.349 | 0.430 |
| Mean $SaO_2$ at T4 | 93.4 | 91.9–94.5 | 92.6 | 91.2–94.3 | 93.8 | 92.6–94.7 | 0.258 | | |
| Minimum $SaO_2$ at T0 | 81.0 | 77.0–85.8 | 80.0 | 76.0–85.0 | 83.8 | 79.5–86.5 | 0.170 | | |
| Minimum $SaO_2$ at T2 | 82.5 | 79.0–86.0 | 84.0 | 80.5–86.5 | 81.0 | 78.5–85.0 | 0.301 | 0.352 | 0.073 |
| Minimum $SaO_2$ at T4 | 84.5 | 81.0–87.8 | 84.5 | 81.0–87.3 | 84.5 | 81.3–87.8 | 0.798 | | |

Values are presented as median and interquartile range (IQR, 25%–75%), except for REI Δ variables, which are mean and SD. Between- and within-group differences were analyzed with the Mann-Whitney and Wilcoxon tests, respectively. These differences were not significant at $P < 0.05$. T0 ($n = 42$) is baseline, T2 ($n = 42$) is after 4 wk of first oral appliance (OA) use, and T4 ($n = 36$) is after 4 wk of second OA use.
BP, bilateral-thrust, permits-opening device; MR, midline-traction, restricts-opening device; REI, respiratory event index (number/h); $SaO_2$, oxygen saturation.

TMA significantly correlated with any other sleep measures at T2 or T4.

*$SaO_2$.* Mean $SaO_2$ at T2 and T4 did not differ significantly from baseline ($P = 0.095$; $P = 0.296$; Appendix Table 1). The 2 OA groups did not differ significantly between T2 and T4 ($P = 0.20$). The entire sample's minimum $SaO_2$ increased from 80% (77.0–85.0) at baseline to 82.5% (79.0–85.0) at T2 and to 84.5% (81.0–87.8) at T4, but neither change achieved statistical significance ($P = 0.551$ and $P = 0.058$). The within-group changes also did not attain significance for the MR-BP and BP-MR groups, respectively.

*ESS.* Overall, the average ESS score was 10.40 ± 5.40 at baseline, which decreased significantly at T2 (7.32 ± 5.38; $P = 0.022$) and T4 (5.96 ± 4.37; $P = 0.001$), but no significant differences between the OA types.

*SF-36 Health Survey.* The SF-36 Health Survey's physical component summary (PCS) and mental component summary (MCS) were significantly improved at T2 and T4 compared with baseline ($P \leq 0.002$). No statistical differences were found between T2 and T4 SF-36 variables of interest and between sex and OA type (Appendix Table 2).

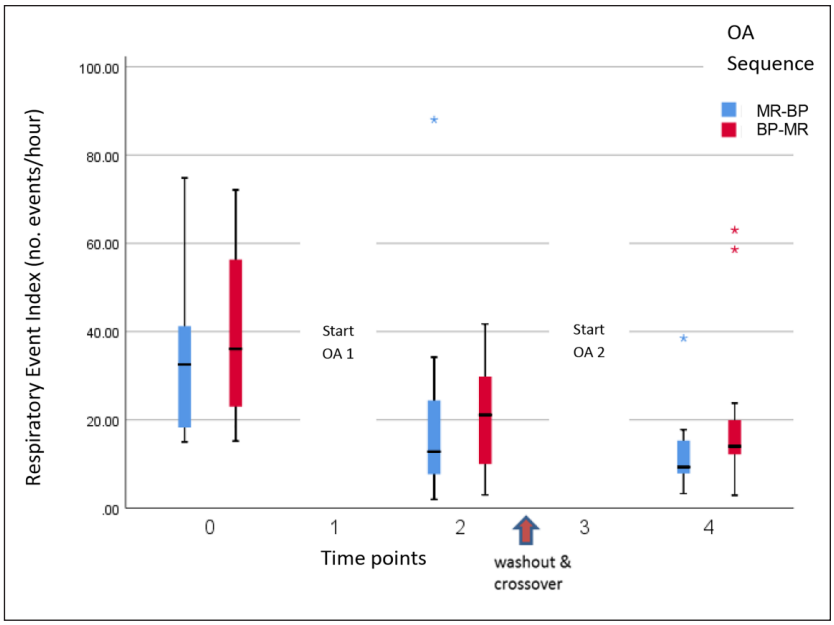


**Figure 2.** Box plots of respiratory event index (REI) by oral appliance (OA) assignment group. Asterisks are extreme outliers. Differences in medians between baseline (0) and all other time points are highly significant within each OA sequence group ($P < 0.001$); between-group differences are not significant at any time point ($P \geq 0.152$), nor are differences between time points 2 and 4 ($P \geq 0.512$). Similarly, mean REI change values did not differ between oral appliance therapy groups over the T0 to T2 interval ($P = 0.929$) or from T0 to T4 ($P = 0.853$).

## Discussion

The study's key findings in subjects who completed the study protocol after 9 wk are as follows: 1) MR and BP OAs demonstrated equivalence in REI attenuation regardless of differences in jaw-opening limitations, 2) both designs significantly reduced the REI in adults with moderate and severe OSA, 3) those with severe OSA showed a more profound REI reduction in terms of both percentage and slope compared to those with moderate OSA, 4) either REI <10 events/h or 50% REI reduction criteria identified OA responders and nonresponders, 5) both OAs demonstrated equivalence and predictability in REI attenuation using either of the 2 criteria, 6) baseline OJ was significantly correlated with mandibular advancement, and 7) ESS and SF-36 QoL scores improved at 4 wk of OA use.

Dentists play a major role in screening for OSA and using OAT in combination with follow-up monitoring to assess treatment efficacy (American Dental Association, House of Delegates 2019). However, OA design and predictability remained questionable regarding their effectiveness in patients with severe OSA. The OA design question addressed here pertains to whether adjustable OATs with the specific feature of limited mouth opening (i.e., limited mandibular movement) affect OA efficacy. Meurice et al. (1996) reported that mouth opening increases upper airway collapsibility due to increased critical pressure and could contribute to OSA event increases. We demonstrated that 2 widely used OA designs (MR that prevents mouth opening and BP, with more freedom of mandibular movement) were effective in significantly improving the REI in most participants who self-titrated these custom, dentist-fitted OAs for 4 wk. This unexpected finding of equivalence of reducing REI could be explained by possible persistent mouthbreathing through unsealed lips with both designs, which was not assessed and is a limitation of the study. Our results are consistent with the Norrhem and Marklund (2016) pilot study, which used elastic bands to minimize mouth opening with another bilateral-thrust OA.

A novel finding was the variability in REI values at the end of the 9-wk study that was dramatically less than T2 and especially from baseline. The interquartile range for all participants combined reduced from approximately 32 at T0 to 21 at T2 to 8 at T4 (same pattern in both OA sequence groups). This suggests that practitioners will find both designs reasonably predictable and efficacious: after 2 mo of self-titration, about half of all users will have an REI between 8 and 16 events/h; a quarter will do better and a quarter worse. Regression analysis by OSA severity indicates that about 50% of the variability in response can be explained by OA usage in the severe group, but as little as 8% in the moderate participants. These experimental findings support the conclusions of a retrospective study (Haviv et al. 2015) that demonstrated that OAT was effective at 2-y follow-up in patients with very severe OSA (AHI >40 events/h) who failed CPAP; their finding is augmented by showing predictability of OA responses in those with severe OSA, regardless of OA design.

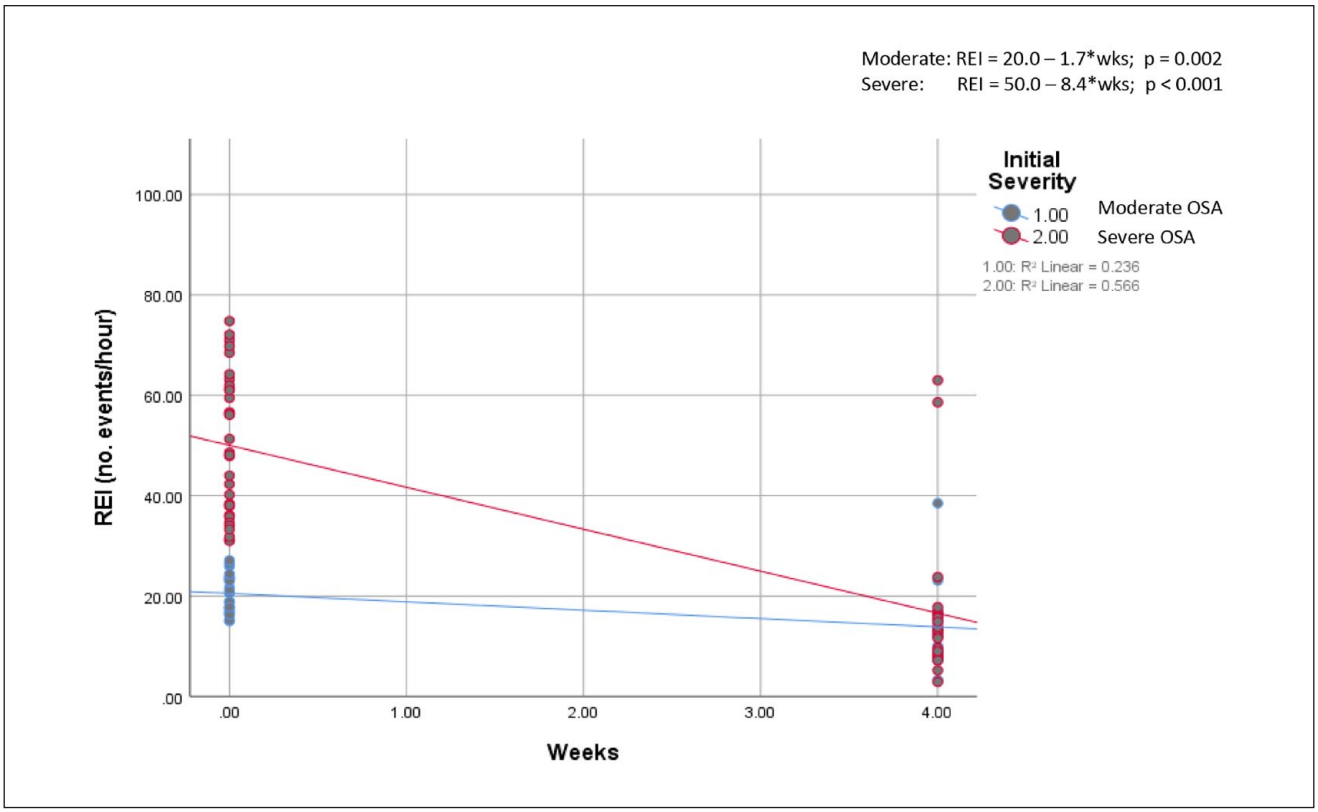


**Figure 3.** Respiratory event index change in participants with moderate and severe OSA from baseline (T0) to T4 (i.e., after second 4 wk of OA use).

Our data support other reports investigating OA use as treatment options for moderate and severe OSA, their effectiveness, and patient preference (Mehta et al. 2001; Ghazal et al. 2009). This report adds to the literature by showing that in these populations, either MR or BP design, when self-titrated for a month, can effectively halve the REI, particularly in severe OSA, based on this study's regression analysis. This finding has important clinical implications for dentists offering custom-fitted OAT for patients with severe OSA, as these showed greater reductions in REI versus in moderate OSA.

Overjet at baseline was significantly associated with the amount by which the subjects could advance their mandibles after 4 wk of OA usage. Not surprising, those with the most pronounced OJs advanced their mandibles the most. The finding of a significant association between snoring reduction and OJ severity over the second leg of the study requires additional investigation for its clinical utility.

Although we did not find differences in efficacy between the 2 designs, when self-titrated over a short period of 4 wk, the results suggest that both designs improve upper airway function and stability, reduce its collapsibility, and increase oropharyngeal space. Collectively, our data suggest self-titrated OAs can be routinely offered as a treatment option for OSA patients, and clinicians can expect about a 50% response rate and to bring the REI down to about 8 to 16 events/h after 8 wk, including those with severe OSA. The improved ESS and SF-36 QoL scores at T2 and T4 demonstrate that OAT effectiveness can be recognized by patients at 4 wk. ESS scores at T4 were below the clinical cutoff for excessive daytime sleepiness. SF-36 QoL score increases at T2 and T4 support OAT use in patients with moderate or severe OSA to also improve their self-reported quality of life at 4 wk.

Study strengths include 1) its randomized crossover design, which eliminated between-subject variability, and 2) testing 2 mechanically different OAs in a sample with an adequate number of severe OSA subjects. Study limitations include use of a 4-wk OAT response window. Previous reports involved titration by a single dentist at regular intervals over 9 to 12 wk, to attain more than an 80% reduction in AHI or fewer than 5 events/h (Hoekema, Stegenga, et al. 2008; Hoekema, Voors, et al. 2008; Holley et al. 2011). Our findings of 70% to 73% REI change at 4 wk in participants with severe OSA are higher than the results of Mehta and coworkers of a 50% REI change after 1 wk of OAT and the 68% AHI reduction reported for patients with very severe OSA at 2-y follow-up (Mehta et al. 2001; Haviv et al. 2015). The 36% dropout rate was mostly due to participants not communicating with the study coordinator. Not monitoring mouthbreathing with OA use was another weakness that may have also limited our ability to detect OA design differences of interest. Those lost to follow-up did not submit their sleep diaries, making it impossible to conclude if intolerance to OAT was the reason for dropping out or to ascertain their OA use time to compare with those who completed the study. It was our experience that a subset of participants might require more time

to self-titrate to an optimally protruded mandibular position. Another group needed constant reminders to self-titrate their OAs, which was beyond the capacity of the staff and the aims of the study. It is possible that some carryover effect (increased laxity of temporomandibular joint ligaments) of the first OA experience occurred in the second phase of the study, but we found no statistical differences between T2 and T4 REI, suggesting our washout period was adequate. A poor understanding of how to self-titrate could have reduced efficacy in some subjects. In future studies, real-time feedback on snoring will be used to increase patient self-titration adherence, since about one-quarter of participants did not advance their OAs beyond the initial 60% setting by the study's end. Our use of the most current SomnoMed OA model and the first-generation TAP might not have provided participants with the most comfortable and state-of-the-art MR TAP OA experience. The rationale for using the first-generation TAP was for comparability with earlier and extensive findings with the exact OA.

In summary, for moderate and severe OSA subjects who completed the study protocol at 8 wk, MR and BP OA designs similarly attenuate REI with greater and predictable reduction in those with severe OSA and concomitant improvement in ESS and SF-36 scores.

## Author Contributions

E. Schneiderman, contributed to conception, design, data acquisition, analysis, and interpretation, critically revised the manuscript; P. Schramm, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; J. Hui, contributed to design, data acquisition, and interpretation, critically revised the manuscript; P.D. Wilson, P. Moura, Z. German, contributed to data acquisition and interpretation, critically revised the manuscript; A. McCann, contributed to data acquisition and analysis, critically revised the manuscript; M. Newton, contributed to data acquisition, critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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